

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

k050574

B. Purpose for Submission:

New 510(k)

C. Measurand:

Hemoglobin A1c in whole blood

D. Type of Test:

Quantitative colorimetric assay where reflectance is read on an instrument.

E. Applicant:

Axis-Shield PoC AS

F. Proprietary and Established Names:

Afinion HbA1c

Afinion HbA1c Control

Afinion AS100 Analyzer

G. Regulatory Information:

1. Regulation section:

864.7470, Glycosylated hemoglobin

862.1660, Single (specified) Analyte Controls

862.2400, Densitometer/Scanner (Integrating, Reflectance, TLC,
Radiochromatography) for clinical use

2. Classification:

Class II, I (reserved because it is an assayed control), and I (reserved because it is
analyzing a class II analyte)

3. Product code:
LCP, JJX, and JQT respectively

4. Panel:
81 (Hematology and Pathology), 75 (Chemistry), and 75, respectively

H. Intended Use:

1. Intended use(s):

See indications for use.

2. Indication(s) for use:

Afinion™ AS100 Analyzer System, consisting of Afinion™ AS100 Analyzer, Afinion™ Test Cartridges and Afinion™ Controls is for in-vitro diagnostic use only. Afinion™ AS100 Analyzer is a compact multi-assay analyzer for point-of-care testing, designed to analyze the Afinion™ Test Cartridges.

Afinion™ HbA1c is an in-vitro diagnostic test for quantitative determination of glycated hemoglobin (% hemoglobin A1c, % HbA1c) in human whole blood. The measurement of % HbA1c is recommended as a marker of long-term metabolic control in persons with diabetes mellitus.

Afinion™ HbA1c Controls have been designed for use with the Afinion™ AS100 Analyzer System. Quality control using the Afinion™ HbA1c Control should be done to confirm that the Afinion™ AS100 Analyzer System is working properly and provides reliable results.

3. Special conditions for use statement(s):

The device is for in vitro diagnostic prescription use. It is also intended for Point-of-Care (POC) use.

4. Special instrument requirements:

The reagents may only be used on the Afinion AS100 Analyzer.

I. Device Description:

Afinion AS100 Analyzer

The Afinion™ test system is a closed system consisting of the Afinion™ AS100 Analyzer and the Afinion™ Test Cartridges. The AS100 is a multi-assay analyzer for point-of-care use.

The analyzer utilizes a digital camera and Light Emitting Diodes (LEDs) to perform two kinds of measurements; reflection measurement (amount of light reflected from a membrane)

and transmission measurement (amount of light propagating through a liquid). The analyzer comes to the user already calibrated, and the calibration information is placed on the cartridge bar code.

The analyzer performs optical, electronic and mechanical checks on the capillary tube, the test cartridge, and individual processing steps. If the analyzer detects an error the assay will be interrupted and patient results are not reported. An error message will be displayed. The operator refers to the User Manual for interpretation of the error message.

To perform a test the capillary-like collection device is used to draw up either a patient or control sample. The collection device is inserted into the test cartridge then placed in the cartridge chamber of the analyzer. The lid is closed and the cartridge is transported into the analysis compartment. Test and lot specific information read from the barcode label tells the analyzer how to process the cartridge. The sample and reagents are automatically transferred between the wells of the cartridge. A monochrome solid-state camera monitors the entire process. When the assay is completed, LEDs illuminate the final reaction area, which can be either a colored membrane or a reaction well. The camera detects the reflected or transmitted light, which is converted to a test result and displayed on the screen. When the user accepts the result, the lid opens and the used cartridge is removed and discarded.

Afinion HbA1c Test Cartridge

The cartridge consists of the sampling device and the reagent container. The cartridge has a barcode label with lot specific information and an ID area for the user to record the sample ID.

Reagents contained within the cartridge include:

Conjugate- blue boronic acid conjugate

Membrane tube- tube with a polyethersulfone membrane.

Washing solution- morpholine buffered sodium chloride

Reconstitution reagent- HEPES buffered sodium chloride with lysis and precipitation agents.

Sodium azide is also present (< 0.1%).

Afinion HbA1c Control

There are 2 assayed liquid ready-for-use preparations designed for use on the Afinion Analyzer. They consist of porcine whole blood (Control C I) and human whole blood (Control C II) with stabilizers added.

J. Substantial Equivalence Information:

1. Predicate device name(s):

DCA2000 Hemoglobin A1c Reagent kit.

2. Predicate 510(k) number(s):

k951361

3. Comparison with predicate:

Both devices are for measurement of the same analyte, have the same intended use, utilize whole blood samples, and both are read on an automated instrument. Both utilize single-use cartridges and are calibrated in-house by the manufacturer.

The test principles vary; the candidate device is a colorimetric assay measured by reflectance, whereas the predicate is an immunoassay utilizing latex agglutination. They are analyzed by different instruments. (The predicate uses the DCA 2000 Analyzer.)

K. Standard/Guidance Document Referenced (if applicable):

The sponsor referenced the following guidance document(s) or standards:

NCCLS document EP5-A. Method Comparison of Precision Performance of Clinical Chemistry Devices; Approved Guideline.

L. Test Principle:

Afinion™ HbA1c is a fully automated boronate affinity assay. The test Cartridge contains all of the necessary reagents. The sample is collected with the integrated sampling device and the Test Cartridge is placed in the cartridge chamber of the analyzer. The blood sample is then automatically diluted and mixed with a solution that releases hemoglobin from the erythrocytes. The hemoglobin precipitates. This sample mixture is transferred to a blue boronic acid conjugate, which binds to the cis-diols of glycated hemoglobin. This reaction mixture is soaked through a filter membrane and all precipitated hemoglobin, conjugate-bound and unbound (i.e. glycated and non-glycated hemoglobin) remains on the membrane. Any excess of conjugate is removed with washing reagent.

The analyzer evaluates the precipitate on the membrane. By measuring the reflectance, the blue (glycated hemoglobin) and the red (total hemoglobin) color intensities are evaluated. The ratio between them is proportionate to the percentage of HbA1c in the sample. The % HbA1c is displayed.

The Afinion™ HbA1c is a fully automated boronate affinity assay for the determination of the percentage HbA1c in human whole blood.

Sample collected using the sampling device integrated in the Reagent Cartridge is diluted and mixed with a liquid that lyses the blood cells releasing hemoglobin from the cells. The sample mixture is transferred to a boronic-acid conjugate, which binds to the cis-diols of glycated hemoglobin. The reaction mixture is soaked through a filter membrane and precipitated hemoglobin, glycated and non-glycated remains on the outside of the membrane. Any excess of conjugate is removed with the washing reagent.

The precipitate on the membrane is evaluated by measuring the blue (glycated hemoglobin) and the red (total hemoglobin) color intensity respectively by the Afinion™ AS100 Analyzer, the ratio between them being proportional to the percentage of HbA1c in the sample. The %HbA1c is displayed on the Afinion™ AS100 Analyzer.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were conducted internally by the manufacturer and externally at three physician office sites. Precision studies were modeled from the National Committee for Clinical Laboratory Standards (NCCLS) guideline EP5-A.

Internal study performed at Axis-Shield

Within-run, between-day and total precision were determined for Afinion HbA1c Controls, C I and C II, and two clinical samples. Two times two replicates were analyzed per day of each sample

Within-run, between-day and total precision, expressed as Coefficient of Variation (CV).
N=number of days.

Sample	N	Average % HbA1c	Within run	Between day	Total
Control C I	20	6.5	0.9%	0.6%	1.4%
Control C II	20	9.1	0.6%	0.5%	1.1%
Patient Level 1	17*	5.6	0.9%	0.2%	1.1%
Patient Level 2	20	10.0	0.7%	0.0%	1.1%

* Based on 17 days of analysis due to hemolysis of the sample.

External study

A precision study was performed at three physician office laboratories (site 1-3) on three Afinion™ AS100 Analyzers. Three levels of HbA1c EDTA blood (samples A-C) were analyzed. The study was performed over 10 consecutive days, first 5 days using Lot 1 and the next 5 days using Lot 2. Each day six replicates of the samples were measured.

The external precision validation of the Afinion™ HbA1c assay using the Afinion™ AS100 Analyzer was performed at the three study sites. The study lasted for two weeks, using one Afinion™ HbA1c Test Cartridge lot for each week. Each day six replicates of each of the three EDTA blood samples A, B and C were analyzed at the three study sites. The blood samples were stored at 2-8 °C.

Results from analysis of three blood samples at three physician offices. Within-day, within-site and total variation.

Sample	Lot	Site	Mean % HbA1c (N=6)	Within-day CV (%)	Within-site CV (%)	Total CV (%)
A	1	1	5.0	1.7	1.9	2.5
		2	5.0	2.9	2.9	
		3	4.9	1.5	2.0	
	2	1	5.1	1.1	1.2	2.2
		2	5.0	1.8	2.0	
		3	4.9	1.6	1.8	
B	1	1	6.2	2.4	2.4	2.3
		2	6.1	2.0	2.0	
		3	6.0	1.2	1.4	
	2	1	6.3	1.3	1.8	1.7
		2	6.2	1.2	1.2	
		3	6.2	0.8	0.9	
C	1	1	9.1	1.3	1.4	2.6
		2	8.8	1.4	1.6	
		3	8.7	2.0	1.9	
	2	1	9.1	0.9	1.0	2.0
		2	8.8	1.1	1.0	
		3	8.8	1.1	1.0	

Additional estimates of precision were provided:

Between instrument precision

Two EDTA blood samples, normal and high HbA1c, were analyzed on ten analyzers in six replicates on each Analyzer. The mean % HbA1c and CV for each sample for each analyzer and for all ten analyzers are shown in table 8.5.

Table 8.5. Results from analysis on ten Afinion™ AS100 Analyzers.

Analyzer	Normal sample		High sample	
	% HbA1c	CV (%)	% HbA1c	CV (%)
S0-57	5.2	1.6	10.2	1.3
S0-52	5.1	1.2	10.4	2.6
S0-53	5.1	0.8	10.3	2.8
S0-54	5.3	1.2	10.7	1.7
S0-60	5.2	1.7	10.8	1.3
S0-61	5.2	1.0	10.4	0.8
S0-63	5.2	1.0	10.7	3.4
S0-64	5.3	1.0	10.4	1.4
S0-71	5.3	1.7	10.9	1.5
S0-74	5.1	1.0	10.4	1.6
All	5.2	2.1	10.5	2.8

Lot-to-lot variation

A panel of 16 blood samples with HbA1c values distributed over a clinically important range was used in addition to Afinion™ HbA1c Control C I and C II. The blood samples and controls were analyzed in duplicates using three Afinion™ HbA1c lots on one single Afinion™ Analyzer. The HbA1c results from analysis of the controls and 16 samples analyzed with three Afinion™ HbA1c lots are shown in table 8.6. Two replicates of each sample (R1 and R2) were analyzed with each lot.

Table 8.6. % HbA1c results from three Afinion™ HbA1c lots.

Sample	% HbA1c lot 1		% HbA1c lot 2		% HbA1c lot 3		Mean lot 1, 2 and 3	
	R1	R2	R1	R2	R1	R2	% HbA1c	CV (%)
Control C I	6.3	6.2	6.4	6.5	6.4	6.6	6.4	2.2
Control C II	9.0	9.1	9.3	9.6	9.1	9.3	9.2	2.3
Sample 1	5.5	5.7	5.5	5.6	5.5	5.6	5.6	1.5
Sample 2	9.3	9.2	9.2	9.2	10.0	9.4	9.4	3.3
Sample 3	6.1	6.1	6.0	6.1	6.0	6.1	6.1	0.9
Sample 4	7.9	7.8	7.9	7.8	7.9	8.0	7.9	1.0
Sample 5	9.7	9.9	9.7	10.1	10.3	10.6	10.1	3.5
Sample 6	5.4	5.4	5.4	5.4	5.6	5.5	5.5	1.5
Sample 7	5.2	5.3	5.2	5.3	5.3	5.3	5.3	1.0
Sample 8	10.1	10.2	10.1	10.1	10.2	10.5	10.2	1.5
Sample 9	6.2	6.2	6.3	6.2	6.2	6.2	6.2	0.7
Sample 10	7.9	7.7	7.9	7.8	8.0	7.9	7.9	1.3
Sample 11	7.7	7.7	7.6	7.5	7.8	7.6	7.7	1.4
Sample 12	7.3	7.4	7.2	7.3	7.4	7.3	7.3	1.0
Sample 13	8.5	8.6	8.5	8.5	8.5	8.8	8.6	1.4
Sample 14	9.5	9.4	9.7	9.9	9.8	9.7	9.7	1.9
Sample 15	10.4	10.4	10.3	10.4	10.3	10.5	10.4	0.7
Sample 16	11.4	11.4	11.6	11.5	12.0	11.8	11.6	2.1

Table 8.7. Bias and 95 % limit of agreements calculated using Bland-Altman analysis.

	Lot 1 - Lot 2	Lot 3 - Lot 2	Lot 3 - Lot 1
Bias	0.0 %	1.7 %	1.7 %
95 % Limit of agreement	-2.6 to 2.5 %	-1.9 to 5.2 %	-2.5 to 5.8 %

b. Linearity/assay reportable range:

Afinion™ HbA1c measures the total glycated hemoglobin and the total hemoglobin concentration. The ratio between them is proportional to the % HbA1c of the sample. The Analyzer calculates the ratio, and the test result is displayed as % HbA1c.

Linearity within the analytical range of 4-18 % HbA1c was demonstrated by mixing a sample with a high HbA1c (17.9%) with a sample with a low HbA1c (5.3%). The two native samples were analyzed 6 times, and the intermediate samples were analyzed in

triplicate. A straight line is observed in the regression plot. The correlation coefficient $r^2 = 1.00$, slope = 1.01 and y-intercept = 0.07 % HbA1c.

The sponsor demonstrated that HbA1c levels could be quantitated accurately between 4 and 18% range when the hemoglobin levels ranged from 6-20 g/dL. The goal of the study was to show that samples high and low in % HbA1c, but manipulated to varying Hb concentrations, would give the same % HbA1c result, independent of the Hb concentration. Three samples had their hemoglobin levels manipulated by removing and adding plasma. Their hemoglobin levels ranged between 6.0 and 25 mg/dL, and the % HbA1c levels ranged from 5.6 to 13.3. Samples were analyzed in triplicate CVs of all replicates were less than 1%.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Afinion™ HbA1c is traceable to the IFCC Reference Method for Measurement of HbA1c6. HbA1c values are reported according to NGSP recommendations at DCCT level.

The results from the Afinion™ HbA1c assay are traceable to the International Federation of Clinical Chemistry (IFCC) Reference Method for measurement of HbA1c in human blood. NGSP (National Glycohemoglobin Standardization Program, US) recommends that HbA1c values are reported at DCCT-level (Diabetes Control and Complications Trial, US). The IFCC Working Group on Standardization of HbA1c has established a Master Equation for the Designated Comparison Method (the method used in the DCCT study, referred to as the NGSP Master Equation by the Working Group). This master equation ($\text{NGSP} = 0.9148 \text{ IFCC} + 2.152$) is implemented in the Afinion™ AS100 Analyzer software and the Analyzer displays values at DCCT level.

During manufacturing the Analyzers are calibrated against a reference system. This procedure has been established to ensure that all Analyzers operate within identical tolerance limits.

Test specific calibration data are established for each lot of Test Cartridges and then stored in the barcode label. When the Test Cartridge enters the Analyzer, the integrated camera reads the barcode. The calibration data for the actual lot are transferred to the instrument and used for calculating results. Calibration by the operator is thus not required.

Afinion™ HbA1c meets the performance standards established by NGSP (National Glycohemoglobin Standardization Program, USA).

Afinion™ HbA1c Controls are recommended used for quality control of the Afinion™ HbA1c assay on the Afinion™ AS100 Analyzer. For each lot of controls a target range is assigned. The assigned % HbA1c value is traceable to the IFCC Reference Method.

To assign the HbA1c values each Afinion™ HbA1c Control lot are analyzed according

to:

1. Minimum three bottles of each control
2. Two approved lots of Afinion™ HbA1c Test Cartridges
3. Three Afinion™ AS100 Analyzers

The target value is calculated as the average of all 18 analyzes for each control.

Internal process control, self-test: A self-test is performed during start-up of the Analyzer to ensure that the instrument is operating according to established specifications. The self-test validates:

- Hardware and software integrity
- Test Cartridge transport system
- Liquid transport system
- Camera vision system

If the self-test fails at any point the red LED will start flashing and an information code will be displayed on the touch screen (see “Information codes and troubleshooting”, page 29). If the Analyzer is unable to use the display, only the red LED will be flashing.

When the Analyzer is switched on for a longer period, it will automatically restart once a day to ensure that a self-test is done regularly.

Stability studies are summarized for the controls. The sponsor specifies the method used to analyze the material, environmental storage conditions, frequency of testing, baseline against which measurements are compared, and acceptance criteria for the study. Accelerated studies are being used by the sponsor to estimate the expiration date, however, on-going real time studies are being performed.

d. Detection Limit:

The Afinion™ HbA1c reportable range is 4.0-18.0% HbA1c.

The hemoglobin measuring range is 6-20 g/dL.

e. Analytical specificity:

The following hemoglobin (Hb) variants have been analyzed and found not to affect the Afinion™ HbA1c test result: HbAC, HbAE, HbAD and HbAJ10.

Carbamylated hemoglobin and pre-HbA1c do not affect the Afinion™ HbA1c test result10.

Pre-glycated hemoglobin does not affect the Afinion™ HbA1c result 11.

Interference

A study performed according to the ERL Manufacturer Check Up Certification procedure by ERL technical staff showed that the Hb-variants HbAC, HbAE, HbAD, HbAJ and carbamylated Hb do not interfere with analysis of % HbA1c on Afinion AS100 Analyzer. Blood samples with up to 22 % preglycated hemoglobin (labile form) showed $\leq 5\%$

interference with the % HbA1c results when analyzed with the AfinionTM HbA1c assay.

Effect on quantification by endogenous interfering substances was tested. Bilirubin (0.2 mg/mL), glucose (5.0 mg/mL), lipids (triglycerides; 15.7 mmol/L and cholesterol; 9.1 mmol/L) or fructosamine (680 µmol/L) in EDTA blood samples gave ≤ 2 % interference when analyzed for % HbA1c on the AfinionTM AS100 Analyzer.

Hemolysed samples cannot be analyzed by the AfinionTM HbA1c assay. Samples with a degree of hemolysis above 6 % will result in information code 204 (Hemolysed blood sample) displayed on the AfinionTM AS100 Analyzer and no result will occur. In samples with a low degree of hemolysis (below 6 %) a negligible interference (<4 %) was observed when analyzed with AfinionTM HbA1c.

f. Assay cut-off:

N/A. This is a quantitative assay.

2. Comparison studies:

Comparability of the AfinionTM HbA1c assay to the Bayer DCA 2000® Hemoglobin A1c assay is demonstrated by an internal comparison study performed by Axis-Shield PoC and as part of an external validation study performed at 3 study sites in the Oslo area. Comparison to an HbA1c reference method was performed by the European Reference Laboratory for glycohemoglobin (ERL).

a. Method comparison with predicate device:

The test system was evaluated internally, externally (at three POL sites), and by a second external certifying group (ERL Manufacturer Check Up Certification).

Forty (40) venous EDTA blood samples were analyzed internally on both AfinionTM AS100 Analyzer and Bayer DCA 2000®. The Bland-Altman method comparison showed acceptable agreement with a bias of -0.3 % HbA1c and 95 % limit of agreement from -1.0 to 0.4 % HbA1c.

At three external study sites 75 venous EDTA blood samples were analyzed on both AfinionTM AS100 Analyzer and Bayer DCA 2000®. The linear regression comparison method showed acceptable agreement with; slope = 0.91, y-intercept = 0.2 % HbA1c and $r^2 = 0.96$.

In total capillary and venous EDTA blood samples from 75 donors were analyzed (25 at each site). The final distribution from the three study sites based on the DCA 2000 measurements of the EDTA blood was as follows:

Group 1:	< 7.0 % HbA1c;	32 samples
Group 2:	7.0-9.0 % HbA1c;	28 samples
Group 3:	> 9.0 % HbA1c;	15 samples

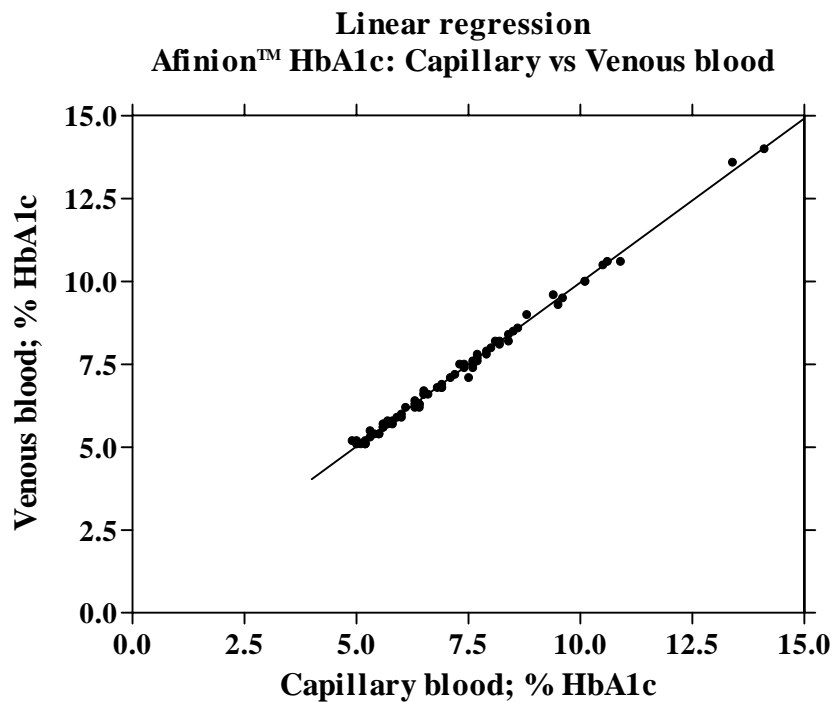
In total 75 patients were included as blood donors. Each donor contributed with one capillary finger prick sample and one venous EDTA sample. The capillary blood samples were analyzed on the Afinion™ AS100 Analyzer and the EDTA venous blood samples were analyzed on both the Afinion™ AS100 Analyzer and on DCA 2000 by the study sites. The samples were analyzed in singleton.

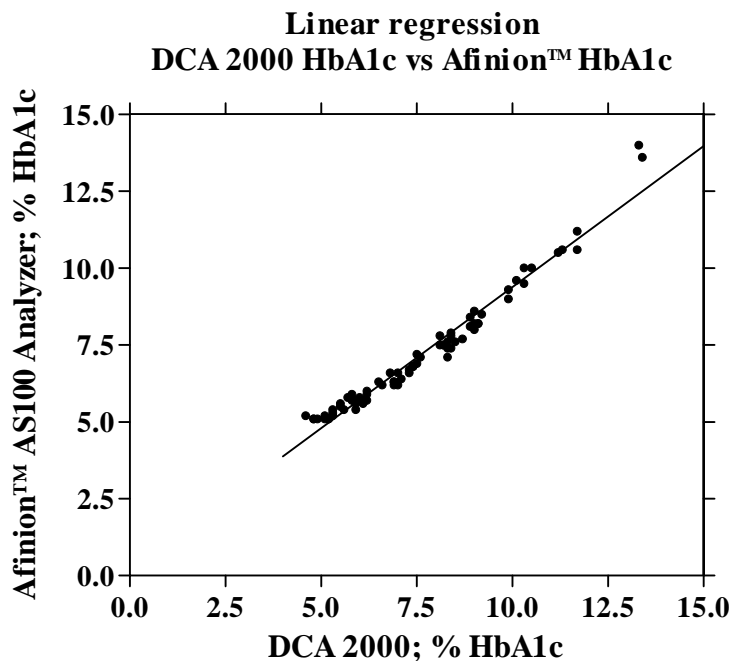
Method comparison. Afinion™ HbA1c (y) vs. another POC system (x). N=number of samples, r=correlation coefficient.

No. sites	N	Regression line	r
3	75	$y=0.91x+0.23$	0.98

Table 2. Capillary vs. EDTA whole blood with Afinion™ HbA1c. N=number of samples, r=correlation coefficient.

No. sites	N	Regression line	r
3	74	$y=0.99x+0.07$	1.00





Capillary and venous blood samples from 74 donors were analyzed externally with the Afinion™ HbA1c assay. The Bland-Altman comparison showed excellent agreement with a bias of 0.0 % and 95 % limit of agreement from -3.5 to 3.6 %. Linear regression; slope = 0.99, y-intercept = 0.1 % HbA1c and $r^2 = 0.99$.

A method comparison study was performed at three physician office laboratories. A capillary finger prick sample and a venous EDTA sample were collected from each donor. The capillary blood samples were analyzed with the Afinion™ AS100 Analyzer. The EDTA venous blood samples were analyzed with both the Afinion™ AS100 Analyzer and with another Point of Care Testing (POCT) system at the study sites (Table 1, 2). The samples were analyzed in singleton.

In a second method comparison study 39 blood samples were analyzed with an affinity HPLC system by ERL. The samples were analyzed by Axis-Shield, using the Afinion™ AS100 Analyzer (Table 3).

Thirtynine (39) venous EDTA blood samples from the European Reference Laboratory for glycohemoglobin (ERL) were analyzed internally by the Afinion™ HbA1c assay and by ERL with their reference method Primus CLC385. The Bland-Altman method comparison showed excellent agreement with a bias of 0.0 % HbA1c and 95 % limit of agreement from -0.3 to 0.3 % HbA1c.

Method comparison. Afinion™ HbA1c (y) vs. an affinity HPLC system (x). N=number of samples, r=correlation coefficient.

N	Regression line	r
39	$y=0.96x+ 0.33$	0.99

ERL Manufacturer Check Up Certification

ERL (European Reference Laboratory) is certified as primary reference laboratory (PRL) and secondary reference laboratory (SRL) in the National Glycohemoglobin Standardization Program (NGSP). The purpose of the NGSP network is to standardize their assays to DCCT (Diabetes Control and Complications Trial) values and to perform certification testing to document traceability to CDDT values.

ERL operates the Afinion system, performs a total of 78 assays on 10 samples. The samples cover a variety of sample variables, e.g., hemoglobin S, hemoglobin C, and low and high hemoglobin values for the purposes of determining the bias and precision of the system. Data is entered and the software automatically issues a certificate. Other evaluations include those for Linearity, interferences, and matrix effects. The calculations performed are described on page 115, and a summary of the performance is on the certificate. Acceptable limits for each parameter appear on page 120. The certificate expires in one year, in this case, January, 2006. The sponsor's certificate appears on page 128, and displays gradings of 4 for excellence and 1 for acceptable.

Two lots were included, and the sponsor evaluated lot to lot variability. The variability is based on the differences between the *mean* differences from each study site, not individual values. Lot variability (between the mean values of the three samples evaluated in the precision studies) were was 0.6, 2.2, and 0.4% for each of the three samples evaluated..

2, 5, and 3 operators participated at each of the three sites.

Patients signed an informed consent. (See page 93.)

b. Matrix comparison:

The assay is intended for several matrices. The sponsor demonstrated equivalence between them by conducting the following study:

The following sample materials can be used with the AfinionTM HbA1c test:

- Capillary blood sample (from finger prick)
- Venous whole blood without anticoagulants
- Venous whole blood with anticoagulants (EDTA, heparin, citrate or NaF)

Capillary samples and EDTA, Heparin, Na-citrate and NaF blood samples were collected from 10 donors. The results show no difference between the capillary and venous blood with different anticoagulants. The recoveries, compared to EDTA, varied between 98-103 % for each donor and anticoagulant. The average recoveries for each anticoagulant were 100-101 % compared to EDTA.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable. Clinical studies are not typically submitted for this device type and matrix.

b. Clinical specificity:

Not applicable. Clinical studies are not typically submitted for this device type and matrix.

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

See expected values, below.

5. Expected values/Reference range:

For methods reporting DCCT traceable values, the upper limit of non-diabetic normal range is approximately 6% HbA1c.

Reference ranges are supported by the certification and standardization procedures performed to validate the assay.

N. Instrument Name:

Afinion AS100 Analyzer

O. System Descriptions:

Definition of Moderate:

The level of concern is moderate if the operation of the software associated with device function directly affects the patient and/or operator so that failures or latent design flaws could result in non-serious injury to the patient and/or operator, or if it indirectly affects the patient and/or operator (e.g., through the action of a care provider) where incorrect or delayed information could result in non-serious injury of the patient and/or operator.

1. Modes of Operation:

This is a random access analyzer, employing reflectance technology. See the Principles section, above.

The Afinion™ Test Cartridges contain all the reagents necessary for the determination of the analyte to be measured. The sample material is collected using the integrated sampling device with a capillary manufactured to draw the exact sample volume from a finger-prick sample or a sample vial. The sampling device is placed directly back into the Test Cartridge before the Test Cartridge is insert into the Afinion™ AS100 Analyzer. The analyzing process is fully automated after inserting the cartridge into the analyzer; the process starts by closing the analyzer lid. Only one cartridge can be run at a time.

All assay and lot specific information necessary for the analyzer to process a test is read from the barcode fixed to the cartridge. All Afinion™ Test Cartridges are single use and shall be disposed after use.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes ____X____ or No _____

The sponsor referenced FDA's Guidance Document for software:
<http://www.fda.gov/cdrh/comp/guidance/1553.html>

Level of Concern: Moderate

The Hazard analysis is performed according to SS-EN ISO 14971, Medical devices - Application of risk management to medical devices.

None of the identified hazards or failure modes are determined to be unacceptable.

The analyzer uses QNX® Neutrino® RTOS version 6.2.1 as operative system.

The application software is written in the following programming languages; C, C++, UML 2.0, ARM assembler and Shell scripts.

No off-the-shelf components besides the operating system are used.

The UML application is responsible for the main functional logic of the analyzer. A Graphical User Interface utilizes the interface to the user. The graphical interface is presented on an LCD display. The user interface with the analyzer is via the touch panel.

Software development processes: Software has been developed and verified according to the model described in the following figure.

All software has been verified and demonstrates compliance with specifications.

3. Specimen Identification:

Samples are identified by manually labeling the cartridge and by logging the patient ID into the analyzer prior to inserting the cartridge into the analyzer, or during the analyzing process. The patient ID cannot be read by the analyzer.

4. Specimen Sampling and Handling:

The sample is collected using the sampling device which is integrated with a capillary manufactured to draw the exact sample volume from a finger-stick or a sample tube. The sampling device is placed back into the test cartridge before it is insert into the analyzer. The sample is automatically transferred into the appropriate multi-well in the cartridge. All further processing of the sample is performed inside the cartridge.

5. Calibration:

The assay is calibrated at the manufacturer's site. Lot specific information is contained on the cartridge. No calibration activities are performed by the user.

Using a series of calibrators, a standard curve is constructed which is lot specific. The calibration information is contained within the barcode which accompanies each reagent unit.

Calibrators are sold with the reagent. Users run the calibrators which are used to construct a standard curve. Unknown values are read from the standard curve.

As part of the analyzer production process, the following areas are calibrated; camera system including light sources, temperature sensors for heating elements and mechanical positions.

The analyzer software includes automatic functions for day-to-day calibration.

Lot-specific calibration per assay is included in the cartridge barcode and read into the analyzer as part of assay processing.

6. Quality Control:

The instrument/assay combination utilizes standard external wet control materials. Additionally, the instrument contains internal checks for detecting electronic, mechanical, and sample problems.

All analyzers are tested prior to release for sale. Quality checks consist of reviewing the data from in-process manufacturing controls, a visual inspection of each analyzer, and functional testing using control material that is traceable to reference material.

Each lot of cartridges is subject to in-process control and release control by use of control

material traceable to reference material.

The analyzer software includes self-test functionality. The self-test is performed at power on or every 24 hours.

The user should perform quality control testing to confirm that the Afinion™ AS100 Analyzer System is working properly and providing reliable results. The users are recommended to analyze controls:

- With each shipment of Afinion™ Test Cartridge.
- With each new lot number of Afinion™ Test Cartridge.
- If the Afinion™ Test Cartridge has not been stored or handled in accordance with specifications
- If an unexpected test result is obtained.
- When training new personnel in correct use of the Afinion™ Test System.
- In compliance with national or local regulations for their facility.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The “Performance Characteristics” Section above:

Human Source Material:

As indicated in the Device Description section (Section I), material used during the manufacturing of the C II control came from a human whole blood. The sponsor indicates that each donor / pooled material was tested and found negative for Human immunodeficiency virus (HIV) 1 and 2, Hepatitis B virus (HBV) and Hepatitis C virus (HCV).

The material was not tested using an FDA licensed or approved assays, but they were tested using assays accredited by the European Community and accredited by the Norwegian government.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.